

CLAIMS:

1. A pharmaceutical dosage form comprising an extended release formulation of the water-soluble drug substance Venlafaxine HCl, comprising a hard gelatin capsule containing a therapeutically effective number of mini tablets comprising of a functional core and/or a functional coating layer or coating film, so that the initial rapid release of the drug substance from the cores is limited.
2. A pharmaceutical dosage form according to claim 1 wherein the cores of the mini tablets are composed of about 10-40% by weight of Venlafaxine HCl, about 40-80% by weight of a gelling agent, about 30-60% by weight of a non-swelling agent, 2-12% by weight of a conjugation agent and 1-30% by weight of classical excipients with the exception of excipients that exhibit disintegrating properties.
3. A pharmaceutical dosage form according to claim 2 wherein the gelling agent is polymer is selected from the group of Hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxycellulose phthalate, poly(ethyleneoxide), polylactic acid, xanthan gum, alginates, sodium and calcium carboxymethylcellulose, carrageen, carbomer, carbopol (oral use), methylhydroxyethylcellulose, propylhydroxyethylcellulose, polyhema, methylcellulose and alginates.
4. A pharmaceutical dosage form according to claim 2 wherein the non-swelling polymer is selected from the group comprising from ethyl cellulose, cellulose acetate propionate, cellulose acetate, poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) 1:2:0.1, commerced as Eudragit RS 100, poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) 1:2:0.2 copolymer, commercially available as Eudragit RL®, polyvinylpyrrolidone acetate, polyvinyl chloride, polyvinyl acetate or polyethylene.
5. A pharmaceutical dosage form according to claim 2 wherein the polymers of the core are conjugated by a pharmaceutically accepted conjugation agent, such as sodium lauryl sulphate, sodium docusate, sodium ceteostearyl sulphate and triethanolamine lauryl sulphate, that causes the decrease on the swelling properties of the core.
6. A pharmaceutical dosage form as defined in claim 1 wherein the cores are partially coated by a functional coating layer, covering one or two surfaces of the core, or one

surface and the perimeter of the core and the thickness of the coating layer ranging between 3-30% of the diameter of the core.

7. A pharmaceutical dosage form as defined in claim 6, wherein the functional coating layer is comprised of a polymer and a water soluble compound, wherein the said polymer and the said water soluble compound are present in a weight ratio of about 1:1 to 9:1.
8. A pharmaceutical dosage form as defined in claim 6, wherein the polymer is either selected from the group consisting of swellable polymers as the ones recited above in claim 3, or from the group consisting of non-swellable polymers, as the ones recited above in claim 4.
9. A pharmaceutical dosage form as defined in claim 6, wherein the water soluble compound is selected either from the group of water soluble salts, such as sodium chloride, sodium bicarbonate or the group of low relative molecular mass organic solid excipients, such as mannitol, lactose, sucrose, sorbitol or citric acid or from the group of water soluble polymers such as polyvinylpyrrolidone, polyvinyl alcohol or low viscosity hydroxypropylmethyl cellulose.
10. A pharmaceutical dosage form as defined in claim 1 wherein the cores are film coated by a functional coating film, that represent about 1.5 to 18% by weight of the weight of the core, applied to a sufficient thickness to reduce the initial release of the drug substance from the said formulation.
11. A pharmaceutical dosage form as defined in claim 10, wherein the functional coating film is comprised of a polymer in a proportion of 10-80% of the dry coating material and a water soluble compound, in a proportion of 20-50% of the dry coating material.
12. A pharmaceutical dosage form as defined in claim 11, wherein the polymer is selected either from the group consisting of swellable polymers such as the ones recited in claim 3, or from the group consisting of non-swellable polymers such as the ones recited in claim 4 or from the group of pH-depended polymers that are insoluble in acidic environments while they soften or dissolve in neutral or basic environments, such as cellulose acetate phthalate, Poly(butyl methacrylate, (2-dimethyl aminoethyl) methacrylate, methyl methacrylate) 1:2:1 copolymer, commercially available as Eudragit E®, poly(ethyl acrylate, methyl methacrylate) 2:1 copolymer, commercially

available as Eudragit 30D®, poly(methacrylic acid, methyl methacrylate) 1:1 copolymer, commercially available as Eudragit L®, poly(methacrylic acid, methyl methacrylate) 1:2 copolymer, commercially available as Eudragit S®.

13. A pharmaceutical dosage form as defined in claim 11, wherein the water-soluble compound is selected from the groups recited above in claim 9.
14. A pharmaceutical dosage form as defined in claim 1 wherein the coating layer or the coating film further comprises a pharmaceutically accepted plasticizer.
15. A pharmaceutical dosage form as defined in claim 1 wherein the coating layer further comprises classical excipients selected from the group of binders, diluents, glidants, lubricants, adhesive agents, opacifiers and colourants.
16. A pharmaceutical dosage form as defined in claim 1 wherein the coating film further comprises classical excipients selected from the groups of and colourants.
17. A pharmaceutical dosage form as defined in claim 1 wherein the coating film is applied from a solution or dispersion of the said polymer and the said water soluble compound in a pharmaceutically acceptable solvent or mixture of pharmaceutically acceptable solvents where the selected constituents of the coating film can be uniformly dissolved or dispersed.
18. A pharmaceutical dosage form as defined in claim 1 wherein the drug substance the gelling agent, the non-swellable polymer and the conjugation agent are wet granulated using a pharmaceutically acceptable solvent or mixture of solvents.
19. A pharmaceutical dosage form as defined in claim 1 wherein the said capsule comprises one to six of the said mini tablets each one containing 25 to 75 mg of the drug substance.
20. A pharmaceutical dosage form as defined in claim 1 wherein linearity between the total weight of the said mini tablets and the strength of the said dosage form is achieved.
21. A pharmaceutical dosage form as defined in claim 1 wherein the dose may be divided by reducing the number of tablets in each capsule.
22. A pharmaceutical dosage form as defined in claim 1, comprising an extended release formulation for once daily administration, which comprises mini tablets partially or

totally coated by a coating layer or coating film that is functional only during the first 2-4 hours of the drug release.

23. A method of preparing a drug delivery system for Venlafaxine which comprises: a) preparing the cores containing Venlafaxine HCl according to claim 5 by a wet granulation, drying and compression process, b) applying a functional coating layer on the cores, according to claim 9, using a direct compression process or applying a functional coating film on the cores using a spraying process, c) encapsulating the prepared mini tablets by using an appropriate encapsulating device.